Infinium™ MethylationEPIC BeadChip
Affordable methylome analysis meets cutting edge content.

Highlights

- **Comprehensive coverage of coding regions and enhancers**
  - Over 850,000 methylation sites per sample at single-nucleotide resolution
- **High assay reproducibility**
  - > 98% reproducibility for technical replicates
- **Simple workflow**
  - PCR-free protocol with the powerful Infinium HD Assay
- **Compatible with FFPE samples**
  - Protocol available for methylation studies on formalin-fixed, paraffin-embedded (FFPE) samples

Introduction

DNA methylation plays an important and dynamic role in regulating gene expression. It allows cells to acquire and maintain a specialized state, suppresses the expression of viral and nonhost DNA elements, and facilitates response to environmental stimuli. Aberrant DNA methylation (hyper- or hypomethylation) and its impact on gene expression have been implicated in many disease processes, including cancer, neurological disorders, aging, and development.¹,²

To enable cost-effective DNA methylation analysis for various applications, Illumina offers a robust methylation profiling platform consisting of proven chemistries and the iScan and NextSeq 550 Systems. The past five years of methyome research, including projects like ENCODE and FANTOM5, have identified enhancer regions as critical sites for differential methylation. The Infinium MethylationEPIC BeadChip (Figure 1) builds on the Infinium HumanMethylation450 BeadChip with > 90% of the original CpGs plus an additional 350,000 CpGs in enhancer regions. By providing quantitative methylation measurement at the single-CpG-site level for normal and formalin-fixed paraffin-embedded (FFPE) samples, this assay offers powerful resolution for understanding epigenetic changes.

Comprehensive genome-wide coverage

The Infinium MethylationEPIC BeadChip provides exceptional coverage of CpG islands, RefSeq genes, ENCODE open chromatin, ENCODE transcription factor binding sites, and FANTOM5 enhancers (Figure 2). Infinium HD technology enables content selection independent of bias-associated limitations often associated with methylated DNA capture methods.

Importantly, the Infinium MethylationEPIC BeadChip contains > 90% of the original Infinium Methylation450 BeadChip content, chosen to provide a broad, comprehensive view of the methylome.

Figure 1: The Infinium MethylationEPIC BeadChip—The Infinium MethylationEPIC BeadChip features > 850,000 CpGs in enhancer regions, gene bodies, promoters, and CpG islands.

The Infinium MethylationEPIC BeadChip targets regions identified by the ENCODE project as potential enhancers. ENCODE tracks for open chromatin, FAIRE assays, and transcription factor binding sites were overlaid to identify the most dynamic regions of the genome for content (Figure 3). Finally, the array targets enhancers identified by the FANTOM5 project across tissue types. The result is a pan-enhancer and coding region view of the methylome that can be used for epigenome-wide association studies on various human tissues and includes the following content categories requested by methylation experts:

- CpG sites outside of CpG islands
- Non-CpG methylated sites identified in human stem cells (CHH sites)
- Differentially methylated sites identified in tumor versus normal (multiple forms of cancer) and across several tissue types
- FANTOM5 enhancers
- ENCODE open chromatin and enhancers
- DNase hypersensitivity sites
- miRNA promoter regions
- > 90% of content on the Illumina HumanMethylation450 BeadChip

Streamlined workflow

The Infinium MethylationEPIC BeadChip follows a user-friendly, streamlined workflow that does not require PCR. Its low sample input requirement (as low as 250 ng), enables analysis of valuable samples derived from limited DNA sources. Infinium MethylationEPIC BeadChip kits contain all required reagents for performing methylation analyses (except for the bisulfite conversion kit, which is available separately).
High-quality data

The Infinium MethylationEPIC BeadChip applies both Infinium I and II assay chemistry technologies (Figure 4) to enhance the density of coverage for methylation analysis. The addition of the Infinium II design allows use of degenerate oligonucleotide probes for a single bead type. This enables each of up to three underlying CpG sites to be either methylated or unmethylated with no impact on the result for the queried site. Illumina scientists rigorously test every product to ensure strong and reproducible performance.

Reproducibility

Reproducibility has been determined based on the correlation of results generated from technical replicates. The Infinium MethylationEPIC BeadChip shows strong correlation between replicates ($r > 0.98$), and with the HumanMethylation450 BeadChip (Figure 6A and 6B). The Infinium HumanMethylation450 BeadChip also shows a high R² correlation with whole genome bisulfite sequencing data (Figure 6C).

Analytical sensitivity

By comparing the results of replicate experiments (duplicates of eight biological samples), Illumina scientists have shown that the Infinium MethylationEPIC BeadChip reliably detects a delta-beta value of 0.2 with a lower than 1% false positive rate.

Internal quality controls

Infinium HD assays produce high-quality data with sample-dependent and independent controls. The Infinium MethylationEPIC BeadChip includes negative controls to account for decreased sequence complexity after bisulfite conversion. The GenomeStudio™ Methylation Module Software has an Integrated Controls Dashboard for easy monitoring of controls. For large-scale studies, the BeadArray Controls Reporter outputs a simple-to-scan excel file for rapid analysis of multiple controls.

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Figure 2: The Infinium MethylationEPIC BeadChip provides dense coverage throughout gene regions — The Infinium MethylationEPIC BeadChip offers broad coverage across gene regions, CpG islands/CpG island regions, shelves, and shores for a comprehensive view of the methylation state.

Figure 3: The Infinium MethylationEPIC BeadChip provides dense coverage throughout enhancer regions — The Infinium MethylationEPIC BeadChip offers dense coverage across multiple content categories requested by methylation experts including enhancer regions.
Integrated analysis software

Infinium MethylationEPIC BeadChip data analysis is supported by the GenomeStudio Methylation Module, enabling researchers to perform differential methylation analysis for small scale studies. GenomeStudio software version 2011.1 features advanced visualization tools that enable researchers to view vast amounts of data in a single graph, such as heat maps, scatter plots, and line plots (Figure 5).

High compatibility with other software

These tools and the GenomeStudio Genome Browser display valuable information such as chromosomal coordinates, percent GC, location in a CpG Island, and methylation b values. For large-scale studies, there are many freely available analysis packages that work in the software framework R for normalization and differential analysis of methylation data.

High cross-application compatibility

Data generated by the Infinium HD methylation assay are easily compatible with data from other Illumina applications, including gene expression profiling. This enables researchers to perform cross-application analysis such as the integration of gene expression data with Infinium MethylationEPIC BeadChip methylation data.

Methylation studies with FFPE samples

Methylation studies on FFPE samples are enabled with a modified version of the Infinium MethylationEPIC BeadChip protocol. This protocol harnesses the Infinium FFPE DNA Restoration Solution to produce robust, reproducible results (Table 1). The Illumina FFPE QC and the Infinium HD FFPE DNA Restore Kits are included. The FFPE DNA Restore Solution and MethylationEPIC BeadChip kits are the same for normal and FFPE samples. Investigators running
Table 1: Comparative Infinium methylation data quality metrics standard vs. FFPE

<table>
<thead>
<tr>
<th>Infinium MethylationEPIC BeadChip</th>
<th>Standard protocol</th>
<th>FFPE protocol</th>
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<tbody>
<tr>
<td>Reproducibility (technical replicates)</td>
<td>$r^2 \geq 98%$</td>
<td>$r^2 \geq 98%$</td>
</tr>
<tr>
<td>Number of sites detected</td>
<td>$\geq 96%$</td>
<td>$\geq 90%$</td>
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</tbody>
</table>

a. Based on noncancer samples, recommended sample input amounts of high-quality DNA as confirmed by PicoGreen and following all other Illumina recommendations as per User Guides.

Synergy with TruSeq™ Methyl Capture EPIC

The panel included in the TruSeq Methyl Capture EPIC Library Prep Kit, an enrichment-based bisulfite sequencing method, mirrors and expands upon the content of the Infinium MethylationEPIC BeadChip. Researchers can move easily between array and sequencing technologies, taking advantage of the low price point on the Infinium MethylationEPIC BeadChip for large-scale screens and diving deep on specific samples or subsets with the TruSeq Methyl Capture EPIC Library Prep Kit. These combined technologies represent the best of both worlds of methylation analysis.

Summary

The Infinium MethylationEPIC BeadChip offers a unique combination of comprehensive, expert-selected coverage, high sample throughput capacity, and affordable price that makes it an ideal solution for large sample-size, genome-wide DNA methylation studies.

Ordering Information

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<thead>
<tr>
<th>Product</th>
<th>Description</th>
<th>Catalog No.</th>
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<tbody>
<tr>
<td>Infinium MethylationEPIC BeadChip Kit (16 Samples)</td>
<td>Each package contains 2 BeadChips and reagents for analyzing DNA methylation in 16 human DNA samples.</td>
<td>WG-317-1001</td>
</tr>
<tr>
<td>Infinium MethylationEPIC BeadChip Kit (32 Samples)</td>
<td>Each package contains 4 BeadChips and reagents for analyzing DNA methylation in 32 human DNA samples.</td>
<td>WG-317-1002</td>
</tr>
<tr>
<td>Infinium MethylationEPIC BeadChip Kit (96 Samples)</td>
<td>Each package contains 12 BeadChips and reagents for analyzing DNA methylation in 96 human DNA samples.</td>
<td>WG-317-1003</td>
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Learn More

To learn more about the product, visit www.illumina.com/products/by-type/microarray-kits/infinium-methylation-epic.html

References


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